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**Feeding management before gastrointestinal studies in pigs**

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## **Abstract**

Pigs are used to model humans in gastrointestinal studies because of their comparable size, physiology and behaviour: both are monogastric omnivores. A porcine surgical model for testing novel, tethered ultrasound capsule endoscopes (USCE) required a clean, motile small intestine. Recommendations for human gastrointestinal tract preparation before the mechanically similar process of video capsule endoscopy describe using oral purgatives while high carbohydrate drinks are recommended before colorectal surgery. Reports of gastrointestinal preparation of pigs exist but lack technical details i.e. administration, efficacy, side-effects.

This report details feeding a high-energy liquid diet to eleven female pigs undergoing surgery and USCE which was readily accepted, easily administered, produced a clean, motile small intestine and caused no detectable physiological/behavioural abnormalities.

## **Keywords**

Pigs, Anaesthesia, Food Withdrawal, Refinement, Gastrointestinal Tract, Capsule Endoscopy, Colorectal Surgery

## Introduction

Preparatory measures before gastrointestinal (GI) endoscopy aim to provide a view of the intestinal mucosa unobscured by turbid liquid or food material, both of which reduce diagnostic value.<sup>1</sup> Similar measures reduce post-surgical complications such as wound dehiscence or anastomotic leakage.<sup>2</sup> Pigs and humans are both monogastric omnivores and similar pre-endoscopic preparation should be required, but opinions regarding pre-procedural preparation for video capsule endoscopy (VCE) remain divided.

In humans, overnight provision of a liquid diet does not worsen small intestinal conditions compared to oral purgatives (sodium picosulphate/magnesium sulphate or polyethylene glycol)<sup>1</sup> which are used for mechanical bowel preparation to empty the GI tract of faeces. However, oral purgative administration is not routine before VCE; preparation should be guided by patient/clinical requirements<sup>3</sup> and consideration of pre-existing co-morbidities and peri-operative antibiosis are considered more important in avoiding complications.<sup>2</sup>

Comparable pre-operative preparation for laboratory pigs is sparsely described and lacks technical details.<sup>4</sup> Complan® (liquid meal replacer) has been used to prepare pigs' GI tract before endoscopic surgery<sup>5</sup> and a combination of an "electrolyte-rich

liquid” and mechanical bowel preparation has been used before anastomotic surgery in minipigs. <sup>6</sup> Both methods were used for 48 hours pre-surgery without complications/results reported.

A clean, empty yet motile bowel was desired in terminally anaesthetized pigs in studies involving stomata formation and ultrasound capsule endoscopy (USCE) <sup>7</sup> prototype testing. Here, the development of a method using a high-energy liquid diet to prepare commercial pigs is detailed.

## **Materials and Methods**

Following ethical approval by Roslin Institute's AWERB, studies were conducted under PPL:PF5151DAF. Eleven female, commercial hybrid pigs, body mass 47 [35 – 50] kg, age 14 [11 – 14] weeks were delivered < 7 days before study. Pigs were pair-housed without straw or ingestible bedding. Rubber matting and heat lamps were used to maintain environmental conditions, which were enriched with dog toys and traffic cones.

A commercially available “dietetic feed source” (“Glutalyte®”; Norbrook, Newry) for use in calves with digestive disturbances was the chosen liquid diet. Prepared according to the manufacturer’s recommendations, it was provided in shallow troughs from arrival so accustomisation could occur. Initially 2 L was offered to each pen (2

pigs) every 12 hours. Concentrated feed (“ABN Pig Rearer Pellets”; ABN Feeds, Cupar, Fife) was offered twice daily until 36 – 48 hours before anaesthetic induction. After concentrate feeding stopped, Glutalyte® was offered at an increased rate (4 L/pen every 12 hours) until pre-anaesthetic medication was administered (figure 1); water was always available *ab libitum*.

Intramuscular sedation comprising midazolam (0.25 mgkg<sup>-1</sup>; “Hypnovel”, Roche), morphine (0.25 mgkg<sup>-1</sup>; “Morphine Sulphate”, Martindale, Essex) medetomidine (7 µgkg<sup>-1</sup>; “Medetor”, Dechra, Shrewsbury) and ketamine (7 mgkg<sup>-1</sup>; “Ketamidor”, Chanelle) preceded induction/maintenance of anaesthesia with isoflurane (“IsoFlo”; Abbot, Maidenhead) vaporised in medical air/oxygen. Blood glucose (BG) was monitored intermittently during anaesthesia (standard institution practice); after surgery pigs were euthanized using pentobarbital (“Pentoject 20%”; Animalcare, York) without recovery from anaesthesia.

Descriptive statistics are stated as (median [range]).

## **Results**

Anaesthesia duration 5 (4 – 11) hours. Glucose supplementation was required in 1/11 animals when BG = 2.4 mmol L<sup>-1</sup> during surgery (normal > 4.7 mmol L<sup>-1</sup> <sup>8</sup>) but normalised after intravenous supplementation (60 – 300 mg kg<sup>-1</sup> hour<sup>-1</sup>; “Glucose

Intravenous Infusion 50% w/v"; Hameln, Gloucester). The small intestinal lumen was consistently empty of ingesta, and peristaltic motion was observed during surgery. No pigs showed abnormal behaviours prior to anaesthesia. All studies were completed successfully.

## **Discussion/Conclusion**

Providing a liquid diet in preparation for GI surgery helped maintain normal physiology, avoided oral purgatives and caused no observable undesirable effects on the pigs' behaviour.

Initially, replacement of ingestible bedding with rubber mats in 2 m<sup>2</sup> pens caused problems with soiling as pigs lay in faeces-contaminated areas. Doubling pen size and elevating sleeping areas allowed pigs to choose distinct sleeping and dunging areas, greatly improving cleanliness. Provision of robust manipulatable objects contributed to normal behaviour.

Since liquid or electrolyte-rich diets prepare the porcine GI tract adequately for surgery<sup>5,6</sup> and a clear liquid diet provides suitable conditions for VCE in humans,<sup>1</sup> it was decided to base GI preparation on a liquid diet. Mechanical bowel preparation using oral purgatives was avoided as their usefulness is questionable<sup>1,3</sup> and can cause adverse side effects in humans<sup>1</sup>. Bowel preparation using prolonged food withdrawal

was also undesirable because of adverse welfare effects. Glutalyte® was chosen because of its high content of carbohydrate (75.7% dextrose w/w) and glutamine. Dextrose provides calories without fibre, avoiding accumulation of intraluminal contents, and glutamine is a “conditionally essential” nutrient for enterocytes during periods of stress.<sup>10</sup> Pigs found Glutalyte® palatable, consuming the majority of liquid offered.

Physiological normality and translational relevance were attained in several ways. Blood glucose remained within normal limits in 10/11 pigs, minimising requirements for glucose supplementation and adverse effects of hypo- or hyperglycaemia on GI motility.<sup>9</sup> Gastrointestinal motility was deemed normal/acceptable by investigators throughout the study. The GI lumen was empty, expediting stomata surgery, allowing the USCE prototype an unobscured examination field, and replicating conditions expected in humans.

Limitations included: lack of a control group, no measurement of Glutalyte® intake/pig and no specific assessment was undertaken regarding behavioural changes potentially associated with an impoverished environment. Only female pigs were used according to the demands of the primary study.



Providing a high carbohydrate liquid diet to pigs as the sole energy source for 36 – 48 hours before gastrointestinal surgery and USCE produced a clean, motile small intestine which was suitable for the experiment performed. With appropriate environmental adaptation, pigs demonstrated neither adverse behaviours nor physiological abnormalities. Therefore, this proved a successful way to prepare laboratory pigs for gastrointestinal surgery and capsule endoscopy studies whilst avoiding aversive procedures i.e., purgative administration and food withdrawal.

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#### Ethical Statement

This study reports technical details of the non-regulated husbandry and preparation of animals undergoing subsequent regulated procedures.

#### Declaration of Conflicting Interests

The authors declare no potential conflicts of interest with respect to research, authorship, and/or publication of the article.

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